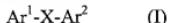


WHAT IS CLAIMED IS:

1. A method of treating a CCR4-mediated condition or disease in a subject, said method comprising administering to a subject in need of such treatment an effective amount of a compound having the formula:



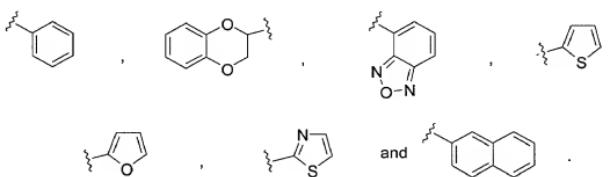
wherein

Ar¹ and Ar² are each members independently selected from the group consisting of substituted or unsubstituted aryl, substituted or unsubstituted fused aryl-heterocyclic ring systems and substituted or unsubstituted heteroaryl; and X is a linking group selected from the group consisting of -N(R)-, -C(O)S-, -CH=CHSO₂- and -SO₂N(R)- wherein R is a member selected from the group consisting of H and substituted or unsubstituted (C₁-C₈)alkyl.

2. A method in accordance with claim 1, wherein X is $-\text{NH}_2$.

3. A method in accordance with claim 1, wherein X is $-\text{SO}_2\text{NH}-$.

4. A method in accordance with claim 1, wherein Ar^1 and Ar^2 are each substituted or unsubstituted members independently selected from the group consisting of:



5. A method in accordance with claim 2, wherein Ar^1 is substituted heteroaryl and Ar^2 is substituted or unsubstituted aryl.

6. A method in accordance with claim 5, wherein said Ar¹ is a substituted heteroaryl selected from the group consisting of substituted thiazolyl, substituted thiienyl, and substituted furanyl.

1 7. A method in accordance with claim 5, wherein said Ar² is a
2 substituted or unsubstituted phenyl or a substituted or unsubstituted naphthyl.

1 8. A method in accordance with claim 3, wherein Ar² is a phenyl
2 group having from 1 to 4 substituents independently selected from the group consisting of
3 halogen, hydroxy, (C₁-C₄)alkyl, (C₁-C₄)alkoxy, (C₁-C₄)alkylthio, (C₁-C₄)haloalkyl, (C₁-
4 C₄)haloalkoxy, nitro, cyano, (C₁-C₄)acyl, amino, (C₁-C₄)alkylamino, and di(C₁-
5 C₄)alkylamino.

1 9. A method in accordance with claim 8, wherein said phenyl group
2 has from 1 to 3 substituents independently selected from the group consisting of halogen,
3 (C₁-C₄)haloalkyl, (C₁-C₄)haloalkoxy, nitro, cyano, and (C₁-C₄)acyl.

1 10. A method in accordance with claim 3, wherein Ar¹ is a substituted
2 or unsubstituted monocyclic or bicyclic heterocycle.

1 11. A method in accordance with claim 10, wherein said heterocycle is
2 selected from the group consisting of pyrrolyl, pyrazolyl, imidazolyl, pyrazinyl, oxazolyl,
3 isoxazolyl, thiazolyl, furyl, thienyl, pyridyl, pyrimidyl, benzothiazolyl, benzoxadiazolyl,
4 purinyl, benzimidazolyl, indolyl, isoquinolyl, quinoxalinyl and quinolyl.

1 12. A method in accordance with claim 11, wherein said heterocycle is
2 selected from the group consisting of thienyl, thiazolyl and benzoxadiazolyl.

1 13. A method in accordance with claim 1, wherein said CCR4-
2 mediated condition or disease is selected from the group consisting of contact
3 hypersensitivity, atopic dermatitis, allergic airway hypersensitivity, allergic rhinitis,
4 atherosclerosis, septic shock, angina, myocardial infarction, restenosis,
5 ischemia/reperfusion injury, multiple sclerosis, rheumatoid arthritis, type I diabetes,
6 psoriasis, cancer and HIV infection.

1 14. A method in accordance with claim 1, wherein said CCR4-
2 mediated condition or disease is psoriasis, contact hypersensitivity or atopic dermatitis.

1 15. A method in accordance with claim 14, wherein said CCR4-
2 mediated condition or disease is psoriasis.

1 **16.** A method in accordance with claim **14**, wherein said CCR4-
2 mediated condition or disease is contact hypersensitivity.

1 **17.** A method in accordance with claim **14**, wherein said CCR4-
2 mediated condition or disease is atopic dermatitis.

1 **18.** A method in accordance with claim **1**, wherein said CCR4-
2 mediated condition or disease is a disease of the airway.

1 **19.** A method in accordance with claim **18**, wherein said disease of the
2 airway is selected from the group consisting of allergic asthma and allergic rhinitis.

1 **20.** A method in accordance with claim **18**, wherein said disease of the
2 airway is allergic asthma.

1 **21.** A method in accordance with claim **1**, wherein said CCR4-
2 mediated condition or disease is a disease of innate immunity.

1 **22.** A method in accordance with claim **21**, wherein said disease of
2 innate immunity is septic shock.

1 **23.** A method in accordance with claim **1**, wherein said CCR4-
2 mediated condition or disease is atherosclerosis.

1 **24.** A method in accordance with claim **1**, wherein said CCR4-
2 mediated condition or disease is a disease or condition characterized by platelet
3 aggregation or thrombosis.

1 **25.** A method in accordance with claim **24**, wherein said CCR4-
2 mediated disease or condition is selected from the group consisting of angina, myocardial
3 infarction, restenosis, stroke and ischemia/reperfusion injury.

1 **26.** A method in accordance with claim **1**, wherein said CCR4-
2 mediated condition or disease is an allergic condition and said compound is used alone or
3 in combination with at least one therapeutic agent wherein said therapeutic agent is an
4 antihistamine.

1 **27.** A method in accordance with claim 1, wherein said CCR4-
2 mediated disease or condition is psoriasis and said compound is used alone or in
3 combination with at least one therapeutic agent selected from a corticosteroid, a lubricant,
4 a keratolytic agent, a vitamin D₃ derivative, PUVA, or anthralin.

1 **28.** A method in accordance with claim 1, wherein said CCR4-
2 mediated disease or condition is atopic dermatitis and said compound is used alone or in
3 combination with at least one therapeutic agent selected from a lubricant and
4 corticosteroid.

1 **29.** A method in accordance with claim 1, wherein said CCR4-
2 mediated condition or disease is asthma and said compound is used alone or in
3 combination with at least one therapeutic agent selected from a β 2-agonist and a
4 corticosteroid.

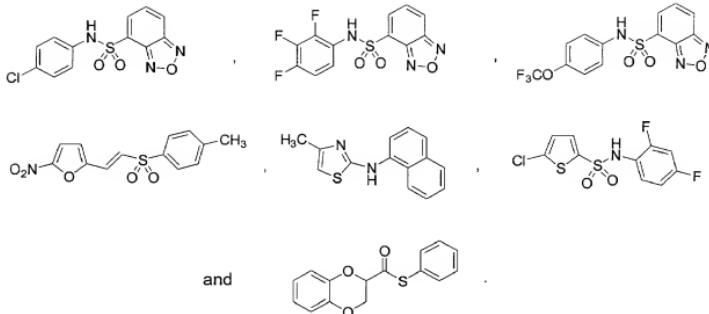
1 **30.** A method in accordance with claim 1, wherein said compound
2 interferes with the interaction between CCR4 and a ligand.

1 **31.** A method in accordance with claim 1, wherein said administration
2 is oral or intravenous.

1 **32.** A method in accordance with claim 1, wherein said subject is
2 selected from the group consisting of human, rat, dog, cow, horse, and mouse.

1 **33.** A method in accordance with claim 1, wherein said subject is
2 human.

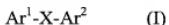
1 **34.** A method in accordance with claim 1, wherein said compound is
2 selected from the group consisting of



35. A method in accordance with claim 1, wherein said CCR4-
 1 mediated disease or condition is selected from the group consisting of multiple sclerosis,
 2 rheumatoid arthritis, type I diabetes, psoriasis, cancer and HIV infection; Ar¹ is a
 3 substituted heterocycle; X is -SO₂NH-; and Ar² is a substituted phenyl.

36. A method in accordance with claim 1, wherein said CCR4-
 1 mediated disease or condition is selected from the group consisting of multiple sclerosis,
 2 rheumatoid arthritis, type I diabetes, psoriasis, cancer and HIV infection; Ar¹ is a
 3 substituted heterocycle; X is -NH-; and Ar² is naphthyl.

37. A pharmaceutical composition for the treatment of a CCR4-
 1 mediated disease or condition, said composition comprising a pharmaceutically
 2 acceptable carrier and an effective amount of a compound which inhibits the binding of
 3 MDC or TARC to CCR4, said compound having the formula:
 4



5 Ar¹ and Ar² are each members independently selected from the group consisting
 6 of substituted or unsubstituted aryl, substituted or unsubstituted fused aryl-
 7 heterocyclic ring systems and substituted or unsubstituted heteroaryl; and
 8 X is a linking group selected from the group consisting of -N(R)-, -C(O)S-,
 9 -CH=CHSO₂- and -SO₂N(R)- wherein R is a member selected from the
 10 group consisting of H and substituted or unsubstituted (C₁-C₈)alkyl.

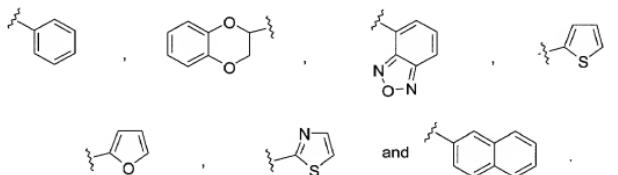
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38. A composition of claim 37, wherein X is -NH-.

12

39. A composition of claim 37, wherein X is -SO₂NH-.

1 **40.** A composition of claim 37, wherein Ar¹ and Ar² are each
2 substituted or unsubstituted members independently selected from the group consisting
3 of:



1 **41.** A composition of claim 37, wherein Ar¹ is substituted heteroaryl
2 and Ar² is substituted or unsubstituted aryl.

1 **42.** A composition of claim 41, wherein said Ar¹ is a substituted
2 heteroaryl selected from the group consisting of substituted thiazolyl, substituted thienyl,
3 and substituted furanyl.

1 **43.** A composition of claim 41, wherein said Ar² is a substituted or
2 unsubstituted phenyl or a substituted or unsubstituted naphthyl.

1 **44.** A composition of claim 41, wherein Ar² is a phenyl group having
2 from 1 to 4 substituents independently selected from the group consisting of halogen,
3 hydroxy, (C₁-C₄)alkyl, (C₁-C₄)alkoxy, (C₁-C₄)alkylthio, (C₁-C₄)haloalkyl, (C₁-
4 C₄)haloalkoxy, nitro, cyano, (C₁-C₄)acyl, amino, (C₁-C₄)alkylamino, and di(C₁-
5 C₄)alkylamino.

1 **45.** A composition of claim 44, wherein said phenyl group has from 1
2 to 3 substituents independently selected from the group consisting of halogen, (C₁-
3 C₄)haloalkyl, (C₁-C₄)haloalkoxy, nitro, cyano, and (C₁-C₄)acyl.

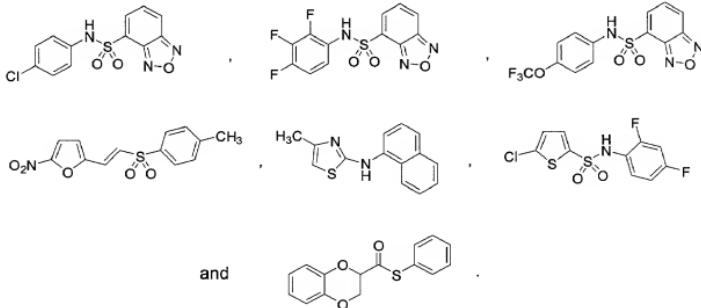
1 **46.** A composition of claim 37, wherein Ar¹ is a substituted or
2 unsubstituted monocyclic or bicyclic heterocycle.

1 **47.** A composition of claim 46, wherein said heterocycle is selected
2 from the group consisting of pyrrolyl, pyrazolyl, imidazolyl, pyrazinyl, oxazolyl,

3 isoxazolyl, thiazolyl, furyl, thienyl, pyridyl, pyrimidyl, benzothiazolyl, benzoxadiazolyl,
4 purinyl, benzimidazolyl, indolyl, isoquinolyl, quinoxaliny and quinolyl.

1 **48.** A composition of claim 47, wherein said heterocycle is selected
2 from the group consisting of thienyl, thiazolyl and benzoxadiazolyl.

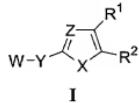
1 **49.** A composition of claim 37, wherein said compound is selected
2 from the group consisting of



1 **50.** A method for modulating CCR4 function in a cell, comprising
2 contacting said cell with a CCR4-modulating amount of a composition of claim 37.

1 **51.** A method for modulating CCR4 function, in which said cell is
2 contacted with a CCR4 protein with a therapeutically effective amount of the composition
3 of claim 37.

1 **52.** A compound of formula (I):



4 or a pharmaceutically acceptable salt thereof, wherein

5 W is selected from aryl, heteroaryl, (C₁-C₈)alkyl, heteroalkyl, cycloalkyl and
6 heterocycloalkyl;

7 X is selected from N(R⁵), S, O, C(R³)=C(R⁴), N=C(R⁴) and, optionally, when Z is
8 N, X can be C(R⁶)(R⁷);

9 Y is selected from a bond, N(R⁵), N(R⁵)-(C₁-C₈)alkylene, O, S and S(O)_n, wherein
10 the integer n is 1 or 2;
11 Z is selected from N and C(R⁸);
12 R¹ and R² are independently selected from H, halogen, CN, CO₂R', CONR'R'',
13 (C₁-C₈)alkyl, heteroalkyl, aryl, heteroaryl, N(R⁶)(R⁷), OR⁹ and optionally,
14 R¹ and R² combine to form a 5- to 8-membered ring containing from 0 to 3
15 heteroatoms selected from N, O and S, wherein R' and R'' are
16 independently selected from H, (C₁-C₈)alkyl and aryl, and when R' and R''
17 are attached to nitrogen atom, they may be combined with the nitrogen
18 atom to form a 5-, 6-, or 7-membered ring;
19 R³, R⁴ and R⁸ are independently selected from H, halogen, CN, OH, (C₁-C₈)alkyl,
20 heteroalkyl, aryl, heteroaryl, O(C₁-C₈)alkyl, N(R⁶)(R⁷) and OR⁹;
21 R⁵ is selected from H, (C₁-C₈)alkyl, heteroalkyl, aryl and heteroaryl;
22 R⁶ and R⁷ are independently selected from H, (C₁-C₈)alkyl, heteroalkyl, aryl and
23 heteroaryl; and
24 R⁹ is selected from (C₁-C₈)alkyl, heteroalkyl and haloalkyl;
25 with the provisos that R² is other than H when W is unsubstituted phenyl, X is S,
26 Y is NH, Z is N and R¹ is (C₁-C₈)alkyl; and R¹ is other than phenyl, when W is phenyl or
27 unsubstituted naphthyl, X is S, Y is NH, and Z is N.

1 **53.** A compound of claim **52**, wherein Z is N.

1 **54.** A compound of claim **52**, wherein X is S.

1 **55.** A compound of claim **52**, wherein Y is N(R⁵).

1 **56.** A compound of claim **52**, wherein Z is N, X is S and Y is N(R⁵).

1 **57.** A compound of claim **52**, wherein W is aryl or heteroaryl.

1 **58.** A compound of claim **57**, wherein W is substituted or unsubstituted
2 phenyl or naphthyl.

1 **59.** A compound of claim **57**, wherein W is substituted or unsubstituted
2 pyridyl or quinolyl.

1 **60.** A compound of claim **52**, wherein R¹ and R² are each
2 independently selected from H and (C₁-C₈)alkyl.

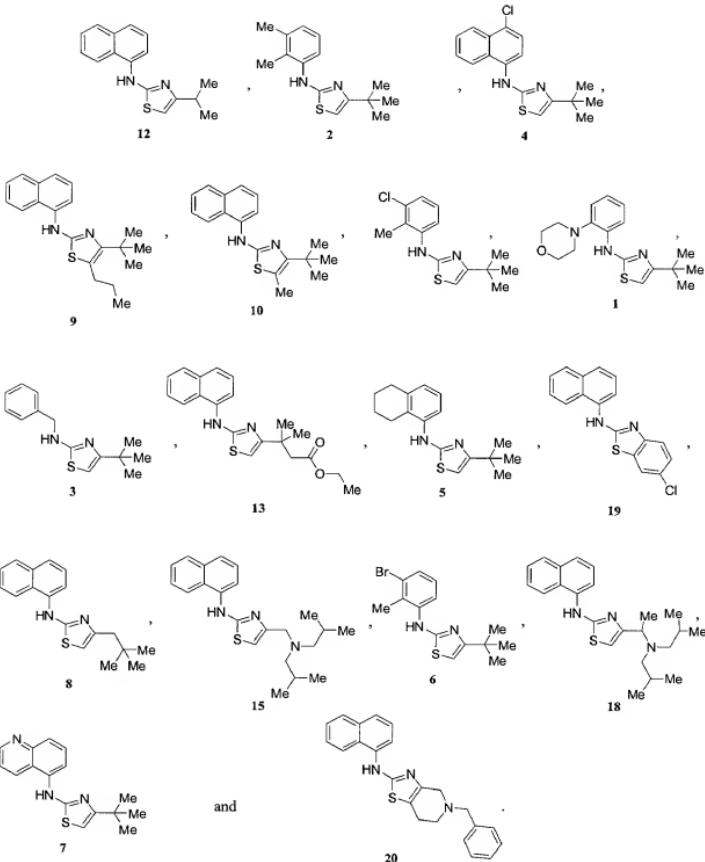
1 **61.** A compound of claim **52**, wherein R¹ and R² are combined to form
2 a fused 6-membered aryl or heteroaryl ring.

1 **62.** A compound of claim **52**, wherein Z is N, X is S, Y is N(R⁵) and
2 R¹ and R² are each independently selected from H and (C₁-C₈)alkyl.

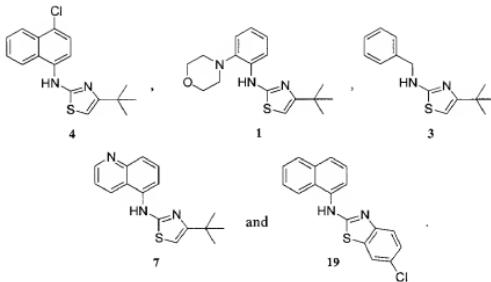
1 **63.** A compound of claim **52**, wherein Z is N, X is S, Y is N(R⁵) and
2 R¹ and R² are combined to form a fused 6-membered aryl or heteroaryl ring.

1 **64.** A compound of claim **52**, said compound being selected from the
2 group consisting of:

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1 65. A compound of claim 52, said compound being selected from the
 2 group consisting of:



66. A compound of claim 52, wherein

W is selected from substituted phenyl, substituted or unsubstituted naphthyl,

pyridyl, quinolyl, (C₁-C₈)alkyl, heteroalkyl, cycloalkyl and heterocycloalkyl;

X is selected from N(R⁵), S, O, C(R³)=C(R⁴), N=C(R⁴) and, optionally, when Z is

N, X can be C(R⁶)(R⁷);

Y is selected from a bond, N(R⁵), N(R⁵)-(C₁-C₈)alkylene, O, S and S(O)_n, wherein the integer n is 1 or 2;

Z is selected from N and C(R⁸);

R¹ and R² are independently selected from H, halogen, CN, CO₂R', CONR'R'',

(C₁-C₈)alkyl, heteroalkyl, aryl, heteroaryl, N(R⁶)(R⁷), OR⁹ and optionally,

R¹ and R² combine to form a 5- to 8-membered ring containing from 0 to 3 heteroatoms selected from N, O and S, wherein R' and R'' are independently selected from H, (C₁-C₈)alkyl and aryl, and when R' and R'' are attached to a nitrogen atom, they may be combined with the nitrogen atom to form a 5-, 6-, or 7-membered ring;

R³, R⁴ and R⁸ are independently selected from H, halogen, CN, OH, (C₁-C₈)alkyl, heteroalkyl, aryl, heteroaryl, O(C₁-C₈)alkyl, N(R⁶)(R⁷) and OR⁹;

R⁵ is selected from H, (C₁-C₈)alkyl, heteroalkyl, aryl and heteroaryl;

R⁶ and R⁷ are independently selected from H, (C₁-C₈)alkyl, heteroalkyl, aryl and heteroaryl; and

R⁹ is selected from (C₁-C₈)alkyl, heteroalkyl and haloalkyl.

67. A compound of claim 66, wherein Z is N.

68. A compound of claim 66, wherein X is S.

69. A compound of claim 66, wherein Y is N(R⁵).

70. A compound of claim 66, wherein Z is N, X is S and Y is N(R⁵).

71. A compound of claim 66, wherein W is substituted phenyl or unsubstituted naphthyl.

72. A compound of claim 66, wherein W is substituted or unsubstituted substituted or unsubstituted quinolyl.

73. A compound of claim 66, wherein R¹ and R² are independently selected from the group consisting of H and (C₁-C₈)alkyl.

74. A compound of claim 66, wherein R¹ and R² are combined to form a membered aryl or heteroaryl ring.

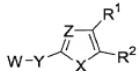
75. A compound of claim 66, wherein W is substituted phenyl or unsubstituted naphthyl, Z is N, X is S, Y is N(R⁵), and R¹ and R² are selected from the group consisting of H and (C₁-C₈)alkyl.

76. A compound of claim 66, wherein W is substituted phenyl or unsubstituted naphthyl, Z is N, X is S, Y is N(R⁵), and R¹ and R² are combined to form a fused 6-membered aryl or heteroaryl ring.

77. A compound of claim 66, wherein W is substituted or unsubstituted substituted or unsubstituted quinolyl, Z is N, X is S, Y is N(R⁵), and R¹ and R² are selected from the group consisting of H and (C₁-C₈)alkyl.

78. A compound of claim 66, wherein W is substituted or unsubstituted substituted or unsubstituted quinolyl, Z is N, X is S, Y is N(R⁵), and R¹ and R² are combined to form a fused 6-membered aryl or heteroaryl ring.

79. A pharmaceutical composition comprising a pharmaceutically active ingredient and a compound of formula (I):



1

or a pharmaceutically acceptable salt thereof, wherein

W is selected from aryl, heteroaryl, (C₁-C₈)alkyl, heteroalkyl, cycloalkyl and heterocycloalkyl;

X is selected from $N(R^5)$, S, O, C(R^3)= $C(R^4)$, N= $C(R^4)$ and, optionally, when Z is
 N, X can be C(R^6)(R^7);

Y is selected from a bond, $N(R^5)$, $N(R^5)-(C_1-C_8)$ alkylene, O, S and $S(O)_n$, wherein the integer n is 1 or 2;

Z is selected from N and C(R^8);

R^1 and R^2 are independently selected from H, halogen, CN, CO_2R' , $CONR'R''$,

(C₁-C₈)alkyl, heteroalkyl, aryl, heteroaryl, N(R⁶)(R⁷), OR⁹ and optionally, R¹ and R² combine to form a 5- to 8-membered ring containing from 0 to 3

heteroatoms selected from N, O and S, wherein R' and R" are independently selected from H, (C₁-C₈)alkyl and aryl, and when R' and R" are attached to nitrogen atom, they may be combined with the nitrogen atom to form a 5-, 6-, or 7-membered ring;

R^3 , R^4 and R^8 are independently selected from H, halogen, CN, OH, (C_1-C_8) alkyl, heteroalkyl, aryl, heteroaryl, $O(C_1-C_8)$ alkyl, $N(R^6)(R^7)$ and OR^9 ;

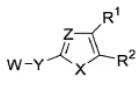
R^5 is selected from H, (C₁-C₈)alkyl, heteroalkyl, aryl and heteroaryl;

R^6 and R^7 are independently selected from H, (C₁-C₈)alkyl, heteroalkyl, aryl and heteroaryl; and

R^9 is selected from (C₁-C₈)alkyl, heteroalkyl and haloalkyl.

80. A method for treating a CCR4-mediated condition

80. A method for treating a CCR4-mediated condition in a subject, said method comprising administering to a subject in need of such treatment an effective amount of compound of formula (I):



I

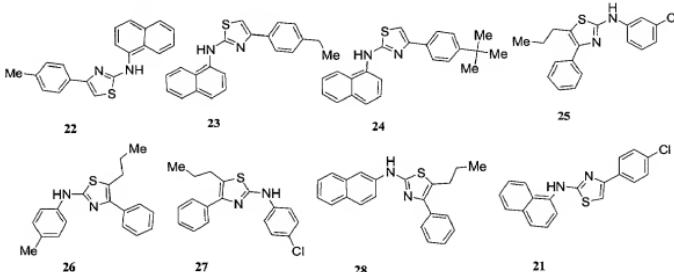
or a pharmaceutically acceptable salt thereof, wherein

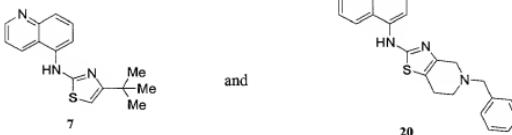
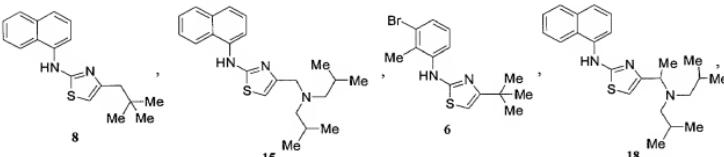
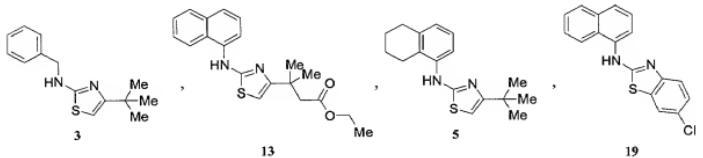
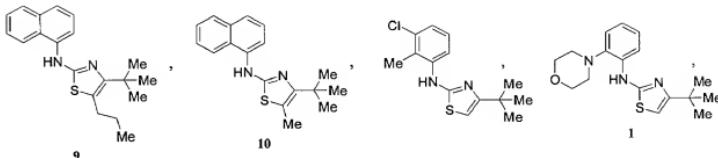
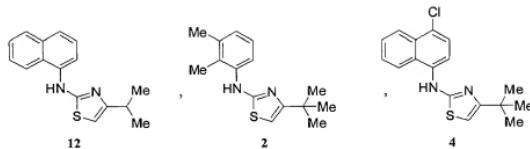
W is selected from aryl, heteroaryl, (C₁-C₈)alkyl, heteroalkyl, cycloalkyl and heterocycloalkyl;

X is selected from $N(R^5)$, S, O, C(R^3)= $C(R^4)$, $N=C(R^4)$ and, optionally, when Z is
 N, X can be $C(R^6)(R^7)$;

11 Y is selected from a bond, N(R⁵), N(R⁵)-(C₁-C₈)alkylene, O, S and S(O)_n, wherein
12 the integer n is 1 or 2;
13 Z is selected from N and C(R⁸);
14 R¹ and R² are independently selected from H, halogen, CN, CO₂R', CONR'R'',
15 (C₁-C₈)alkyl, heteroalkyl, aryl, heteroaryl, N(R⁶)(R⁷), OR⁹ and optionally,
16 R¹ and R² combine to form a 5- to 8-membered ring containing from 0 to 3
17 heteroatoms selected from N, O and S, wherein R' and R'' are
18 independently selected from H, (C₁-C₈)alkyl and aryl, and when R' and R''
19 are attached to nitrogen atom, they may be combined with the nitrogen
20 atom to form a 5-, 6-, or 7-membered ring;
21 R³, R⁴ and R⁸ are independently selected from H, halogen, CN, OH, (C₁-C₈)alkyl,
22 heteroalkyl, aryl, heteroaryl, O(C₁-C₈)alkyl, N(R⁶)(R⁷) and OR⁹;
23 R⁵ is selected from H, (C₁-C₈)alkyl, heteroalkyl, aryl and heteroaryl;
24 R⁶ and R⁷ are independently selected from H, (C₁-C₈)alkyl, heteroalkyl, aryl and
25 heteroaryl; and
26 R⁹ is selected from (C₁-C₈)alkyl, heteroalkyl and haloalkyl.

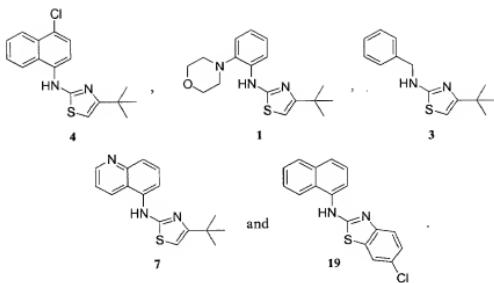
1 81. A pharmaceutical composition comprising a pharmaceutically
2 acceptable carrier and a compound selected from the group consisting of:



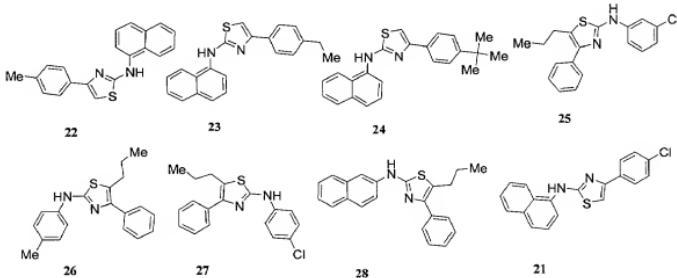


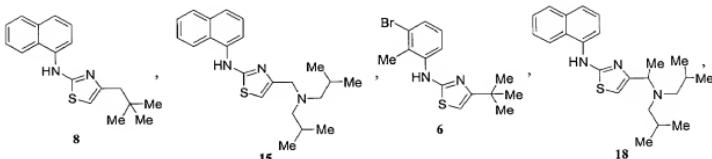
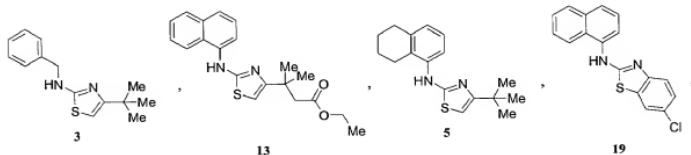
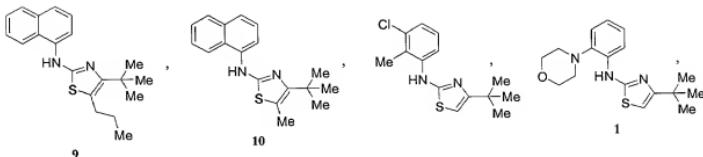
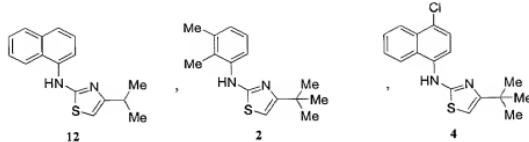
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1 **82.** A pharmaceutical composition of claim 81, wherein said
2 compound is selected from the group consisting of:

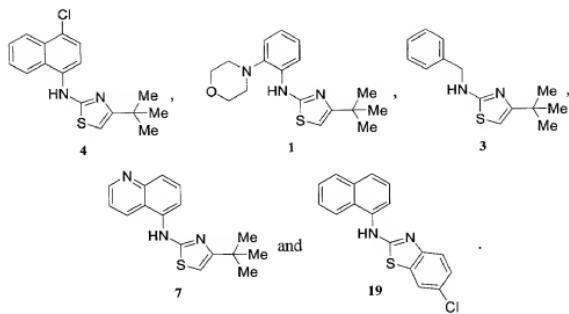


1 **83.** A method for treating a CCR4-mediated condition in a subject, said
2 method comprising administering to a subject in need of such treatment an effective
3 amount of a compound selected from the group consisting of:





1 84. A method in accordance with claim 83, wherein said compound is
2 selected from the group consisting of:



3